Phase I/IIb Trial: In-Situ Vaccine for Metastatic Colorectal Cancer

**Introduction**

The clinical benefits of therapeutic vaccination in the treatment of cancer-metastatic colorectal cancer (mCRC) are limited by the existence of a variety of immunologic roadblocks, such as the presence of tumor-infiltrating lymphocytes that can sequester therapeutic agents and escape immune surveillance (1-3). However, it is critical to elicit host-mediated host vs. tumor (HVT) effect, which involves the rejection of BAG cells to generate a linked tumor-specific immunity.

**Methods**

The trial is designed to evaluate the safety and feasibility of a novel in-situ vaccine platform that is bioengineered to replace the contributions of type 1 cytokine storm. Tumor cryoablation, a strategy for counter-regulating the immunosuppressive and immunosuppressive microenvironment, is employed to potentiate an immunologic response. Cryoablation is performed to create a lesion with a Type 1 environment. In the priming phase, BAG cells are injected intradermally in order to elicit high titers of allo-specific Th1/CTL in circulation. These activated T-cells in turn non-specifically activate circulating NK cells, M1 macrophages and differentiated memory CD4+ Th1 cells with anti-CD3/CD28 microbeads attached that express high density CD40L.

**Dosing Schedule**

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**Discussion**

The novel therapeutic vaccine platform is being tested for its ability to elicit immune-mediated antitumor effects in patients with mCRC. The vaccine is designed to provide a linked host vs. tumor effect. The vaccine is characterized by a combination of BAG cells, cryoablation and a Type 1 cytokine storm. The in-situ vaccine effect caused by the non-specific lysis of tumor cells in a Type 1 cytokine environment can be amplified by the development of tumor-specific Th1/CTL.

**Vaccination Phase**

In the priming phase, BAG cells are injected intradermally in order to elicit high titers of allo-specific Th1/CTL. The vaccine is given in a bioreactor. After 9 days, an intermediate cell is harvested and expressed in a bioreactor. After 9 days, an intermediate cell is harvested.

**Priming Phase**

The vaccine is administered in a bioreactor. After 9 days, an intermediate cell is harvested and expressed in a bioreactor.

**Amplification**

The vaccine is administered in a bioreactor. After 9 days, an intermediate cell is harvested and expressed in a bioreactor.

**Activation and Booster**

The vaccine is administered in a bioreactor. After 9 days, an intermediate cell is harvested and expressed in a bioreactor.